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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/674,962 | 11/08/2000 | Bernhard Hauer | 49041 | 7018 |

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| EXAMINER | |
|---|---|
| WESSENDORF, TERESA D | |
| **ART UNIT** | **PAPER NUMBER** |
| 1639 | |

DATE MAILED: 02/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/674,962 | HAUER ET AL. | |
| | Examiner | Art Unit | |
| | T. D. Wessendorf | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *7-18* is/are withdrawn from consideration.

5)☒ Claim(s) *6* is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *(3) Status of Claims*

Claims 1-18 are pending in the application.

Claims 7-18 are withdrawn from consideration as being drawn to non-elected invention.

Claims 1-6 are under examination.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons advanced in the last Office action.

### *Response to Arguments*

A).- C). The rejection of the claims under these paragraphs has been overcome with the amendments to the claims and applicants' arguments.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Volz et al (Journal of Chromatography) in view of Haymore et al (EP 409,814) and Guerinot et al (5,846,821) for reasons as set forth in the last Office action.

***Response to Arguments***

Applicants admit that Volz et al teach the characterization of the metal-binding domain of the ATPase-
439 and ATPase-948 of Helicobacter pylori (Abstract and page 29, last paragraph). It was possible for Volz et al. to purify said ATPases without using an additional His-tag sequence (see page 29, Abstract, last sentence and page 37, conclusions, last sentence.) Volz et al do not teach anything about a method using the motif HxHxxxCxxC for the purification of other proteins or fusion proteins between said motif and other protein. Since Volz et al. do not discuss a general method of using parts of the

ATPase or the motif for the purification of proteins applicants do not see why the skilled worker would use part of the ATPase of the motif for the purification of proteins.

ln addition, applicants' own studies have shown that these ATPase binding sites display a binding affinity which is too low for efficient purification of all desired proteins(specification page 2, lines 40 to 45). Applicants' sequences bind to immobilized metal ions at least 1.5 times more strongly than the Helicobacter pylori ATPase-439 (page 9, lines 28-32 and page 14, lines 39-46) and are therefore useful for the purification of a lot of proteins. By using the advantageous sequences, it is possible to purify proteins in a very high yield (page 14, lines 43 to 46). Nothing is mentioned about this in Volz et al.

In response, applicants' arguments above appear contradictory. In one instance applicants admit that Volz purify said ATPases. While on the other hand, Volz does not disclose a method using the motif for the purification of other proteins or fusion proteins between said motifs. Applicants' arguments are not commensurate in scope with the claimed compound. The claims recite only compounds. It does not recite a method that purifies other proteins or fusion proteins, albeit, as admitted, Volz discloses purification of ATPase.

As to applicants' statement as to the findings in the specification, is immaterial, as the compound is known and the argued function is a limitation not found in the claims. Furthermore, it is not clear whether the compound with low efficient purification obtained for the ATPase is the compound used by Volz. Accordingly, the compound of Volz renders the claimed prima facie obvious.

Applicants admit that Guerinot et al. teach the discovery of a family of polypeptide, designated as metal-regulated transporter, MRP, polypeptide, which share several structural/functional properties, at least one of which is related to metal transport (see column 2, lines 24-28,

Claims 23 and 24). But argue that The MRT proteins disclosed by Guerinot et al. have four histidine rich domains and the protein fragment is totally different from the claimed protein fragments. Guerinot discloses a general teaching that the amino acids lle and Leu belong to the group of amino acids which have uncharged side chains and therefore a skilled worker would change the codon usage of a given nucleic acid sequence coding for example for Leu to the codon usage of Ile in the event he is interested in mutagenizing the said sequençe without changing the activity of the enzyme encoded by the sequence. These types of changes are only possible as disclosed

by Guerinot et al. in areas which are not essential for the activity of the MRP proteins (see col. 14, lines 30 to 33).

In reply, Guerinot is not employed for the purpose as argued, i.e., for a different protein fragment. Rather, as applicants' recognized for its general teachings, as well known in the art, for the conservative substitutions of Leu with Ile. Whether the substitution occurs in the essential or non-essential part of the protein, as argued, is immaterial as Guerinot positively recites such substitution. Applicants have not shown that such conservative substitutions produce a different result. The under Guerinot applies to Haymore since applicants' used the same argument as with Guerinot.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon hindsight, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Volz positively teaches the claimed compound. Guerinot discloses conservative substitution of Leu for Ile. Thus, the

combined teachings of the references render the claimed prima facie obvious to one having ordinary skill in the art.

As stated in the last Office action, claims 5 and 6 are free of prior art. Claim 6 is allowable.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

This application contains claims 7-18 drawn to an invention nonelected. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
February 7, 2004